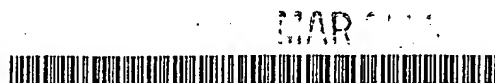


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- (21) International Application Number: PCT/BE2003/000158 (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
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- (71) Applicants (*for all designated States except US*): K.U. LEUVEN RESEARCH AND DEVELOPMENT [BE/BE]; Groot Begijnhof 58-59, B-3000 Leuven (BE). AARHUS UNIVERSITET [DK/DK]; Nordre Ringgade 1, DK-8000 Aarhus C (DK). AARHUS UNIVERSITY HOSPITAL [DK/DK]; Aarhus Amt, Lyseng Allé 1, DK-8270 Højbjerg (DK).
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WO 2004/026330 A1

(54) Title: METHODS AND PREPARATIONS FOR CURING CRITICALLY ILL PATIENTS

(57) Abstract: The present invention pertains to the use of a blood mannan-binding lectin (MBL) regulator for the manufacture of a life saving drug to treat or cure a critically ill patient. It further involves the use of measurements of MBL to predict mortality in critically ill ICU patients. One further aspect of present invention is to the use of monomers and oligomers of MBL in prophylactic and/or curative treatment of patients admitted to intensive care units (ICUs).

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/BE 03/00158

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K38/17 A61P00/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE, EMBASE, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>GARRED PETER ET AL: "Association of mannose-binding lectin polymorphisms with sepsis and fatal outcome, in patients with systemic inflammatory response syndrome." THE JOURNAL OF INFECTIOUS DISEASES. UNITED STATES 1 NOV 2003, vol. 188, no. 9, 1 November 2003 (2003-11-01), pages 1394-1403, XP009024751 ISSN: 0022-1899 the whole document</p> <p style="text-align: center;">-/-</p>	1-48

☒ Further documents are listed in the continuation of box C.

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Date of the actual completion of the international search

28 January 2004

Date of mailing of the international search report

18/02/2004

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/BE 03/00158

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 24919 A (LEUVEN K U RES & DEV ; DEN BERGHE GRETA HERMAN VAN (BE); ZEGHER FRA) 21 September 1995 (1995-09-21) claims 1,5 page 3, line 33 - line 36 examples 1-7 ----	1-9,11, 12, 17-21, 35-38
X	WO 99 64453 A (STATENS SERUMINSTITUT ;LAURSEN INGA (DK)) 16 December 1999 (1999-12-16) claims 24-26 page 17, line 16 - line 34 ----	1-48
X	WO 02 05833 A (FISCHER PER ; NATLMMUNE APS (DK)) 24 January 2002 (2002-01-24) the whole document ----	1-48
X	KILPATRICK DAVID C: "Mannan-binding lectin: clinical significance and applications." BIOCHIMICA ET BIOPHYSICA ACTA. NETHERLANDS 19 SEP 2002, vol. 1572, no. 2-3, 19 September 2002 (2002-09-19), pages 401-413, XP004380529 ISSN: 0006-3002 the whole document in particular 5. p 408-409 ----	1-48
Y	WO 00 24398 A (BRISTOL MYERS SQUIBB CO) 4 May 2000 (2000-05-04) claims 14,15 ----	1-9,11, 12, 17-21, 35-38
Y	HIBBERD M L ET AL: "Variation in the mannose binding lectin (MBL) gene and susceptibility to sepsis" SEPSIS 2001 NETHERLANDS, vol. 4, no. 3, 2001, pages 201-207, XP009024789 ISSN: 1385-0229 page 203, column 2, paragraph 3 -page 204, column 2, paragraph 6 abstract ---- -/--	1-48

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/BE 03/00158

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HANSEN TROELS KRARUP ET AL: "GH strongly affects serum concentrations of mannan-binding lectin: Evidence for a new IGF-I independent immunomodulatory effect of GH" JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, vol. 86, no. 11, November 2001 (2001-11), pages 5383-5388, XP002268239 ISSN: 0021-972X the whole document	1-9, 11, 12, 17-21, 35-38
Y	GARRED P ET AL: "Association of mannose-binding lectin gene heterogeneity with severity of lung disease and survival in cystic fibrosis." THE JOURNAL OF CLINICAL INVESTIGATION. UNITED STATES AUG 1999, vol. 104, no. 4, August 1999 (1999-08), pages 431-437, XP002268240 ISSN: 0021-9738 abstract discussion	1-48
P,X	HANSEN TROELS KRARUP ET AL: "Intensive insulin therapy exerts antiinflammatory effects in critically ill patients and counteracts the adverse effect of low mannose-binding lectin levels." THE JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM. UNITED STATES MAR 2003, vol. 88, no. 3, March 2003 (2003-03), pages 1082-1088, XP009024778 ISSN: 0021-972X the whole document	1-48
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P,Y	WO 03 010188 A (MATTHIESEN FINN ; NATIMMUNE AS (DK)) 6 February 2003 (2003-02-06) claims 37-49 page 25, line 20 -page 26, line 3	1-48

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/BE 03/00158

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,Y	<p>EP 1 344 533 A (NATIMMUNE AS) 17 September 2003 (2003-09-17) page 14, paragraph 141 -page 1, paragraph 150 claims 45-51</p>	1-48

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application

PCT/BE 03/00158

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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PCT/BE.23/00158

Sheet No. 5

Box No. VIII (iv) **DECLARATION: INVENTORSHIP** (only for the purposes of the designation of the United States of America)
The declaration must conform to the following standardized wording provided for in Section 214; see Notes to Boxes Nos. VIII, VIII (i) to (iv) (in general) and the specific Notes to Box No. VIII (iv). If this Box is not used, this sheet should not be included in the request.

Declaration of inventorship (Rules 4.17(iv) and 51bis.1(a)(iv))
for the purposes of the designation of the United States of America:

I hereby declare that I believe I am the original, first and sole (if only one inventor is listed below) or joint (if more than one inventor is listed below) inventor of the subject matter which is claimed and for which a patent is sought.

This declaration is directed to the international application of which it forms a part (if filing declaration with application).

This declaration is directed to international application No. PCT/BE.23/00158 (if furnishing declaration pursuant to Rule 26ter).

I hereby declare that my residence, mailing address, and citizenship are as stated next to my name.

I hereby state that I have reviewed and understand the contents of the above-identified international application, including the claims of said application. I have identified in the request of said application, in compliance with PCT Rule 4.10, any claim to foreign priority, and I have identified below, under the heading "Prior Applications," by application number, country or Member of the World Trade Organization, day, month and year of filing, any application for a patent or inventor's certificate filed in a country other than the United States of America, including any PCT international application designating at least one country other than the United States of America, having a filing date before that of the application on which foreign priority is claimed.

Prior Applications: 23 September 2002 - 0222014.3 - GB

I hereby acknowledge the duty to disclose information that is known by me to be material to patentability as defined by 37 C.F.R. § 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the PCT international filing date of the continuation-in-part application.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

VAN DEN BERGHE Greta

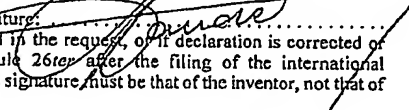
Name: rue de Beaumont 77

Residence: 1390 Grez-Doiceau

(city and either US state, if applicable, or country) Belgium

Mailing Address:

Citizenship: BE

Inventor's Signature:  Date: 06/10/03
(if not contained in the request, or if declaration is corrected or added under Rule 26ter after the filing of the international application. The signature must be that of the inventor, not that of the agent) (of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26ter after the filing of the international application)

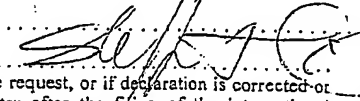
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(city and either US state, if applicable, or country) 8240 Risskov

Mailing Address: Denmark

Citizenship: DK

Inventor's Signature:  Date: 19/10/03
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☒ This declaration is continued on the following sheet, "Continuation of Box No. VIII (iv)".

Continuation of Box No. VIII (i) to (v) **DECLARATION**

If the space is insufficient in any of Boxes Nos. VIII (i) to (v) to furnish all the information, including in the case where more than two inventors are to be named in Box No. VIII (iv), in such case, write "Continuation of Box No. VIII..." (indicate the item number of the Box) and furnish the information in the same manner as required for the purposes of the Box in which the space was insufficient. If additional space is needed in respect of two or more declarations, a separate continuation box must be used for each such declaration. If this Box is not used, this sheet should not be included in the request.

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Denmark

Signatures



Date

22/10/03